PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Richard S. Larson	Group Art Unit: 1644
Serial No.: 09/760,599	Examiner: M Haddad
Filed: January 16, 2001	Atty. Dkt. No.: SCI200/4-1CIP
For: PEPTIDE INHIBITORS OF LFA-1/ICAM-1 INTERACTION	

CERTIFICATE OF EXPRESS MAIL

"EXPRESS MAIL" LABEL NO. EV 022537961 US
DATE OF DEPOSIT: March 10, 2003
I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE United States Postal Service "Express Mail Post Office to Addressee" service on the date indicated above and is addressed to the Assistant Commissioner of Patents, Washington D.C. 20231.

DECLARATION OF RICHARD S. LARSON, M.D., Ph.D.

I RICHARD S. LARSON, HEREBY DECLARE AS FOLLOWS:

1. I am an Associate Professor in the Department of Pathology at the University of New Mexico Health Sciences Center, the Medical Director of the University Rapid Response Laboratory and Director of the Laboratory on Cell Adhesion and Drug Design. I am an expert in the fields of hematopathology, cellular adhesion, protein-peptide interactions, and drug discovery.

2. My expertise is evidenced by the fact that I have: (i) authored over 10 book chapters; (ii) and authored over 60 scientific articles. I am also the inventor of the subject matter of the captioned patent application. I am the recipient of the College of American Pathologist's Lansky Award for my leadership in and contribution to the practice of pathology, University of New Mexico (UNM) Regents Lectureship for contribution to UNM, and American Cancer Society Designated National Investigator for the Coaches against Cancer and Hoops for Lymphoma/Leukemia. One of my publications (Ledford et al, *J Mol Diag*, attached) validated the use of a novel non-DNA amplification platform for determining the presence of DNA mutations. This manuscript was chosen as manuscript of the year and appeared in the 2002 Yearbook of Pathology and Laboratory Medicine. I received both my MD and PhD from Harvard University. I have 18 years of experience in the research of ICAM-1 and

LFA-1. During my PhD work in the 1980s I was one of the original scientists that worked on ICAM-1. I am a co-inventor on the original patent for LFA-1 in 1990.

3. It is my understanding that the Patent Examiner has rejected certain claims in the captioned application on the ground that, although the evidence presented indicates that the claimed peptides would have utility in the treatment of myocardial infarction, the Examiner does not believe there is a reasonable basis that the peptides would also be useful in the treatment of a hematopoietic neoplastic disease, radiation injury, asthma, rheumatoid arthritis, or lymphoma metastasis.

4. It is my opinion that the Examiner is incorrect and that one of skill in this field would have a positive expectation that the cyclic peptides claimed in the application would be effective in treating a number of diseases or conditions that are mediated through the LFA-1/ICAM-1 interaction, including all those listed in paragraph 3, above.

5. Attached to this declaration is a copy of a paper from my laboratory that demonstrates the *in vivo* activity of a claimed cyclic peptide in a model of myocardial infarction in which the LFA-1/ICAM-1 interaction is inhibited by the peptide. Also, as described in the Specification of my patent application, at page 3, line 10, *in vivo* use of mAbs against LFA-1 or ICAM-1 blocks LFA-1 function in a number of disease models. Also attached are references that describe such studies. These models include all of those in the rejected claims. Anyone trained in the field would be able to deduce that the peptide antagonists described in our patent would be useful in these diseases. The following references show the efficacy of mAbs against ICAM-1 or its ligand LFA-1 in the therapy for asthma, stroke, rheumatoid arthritis, leukemia, septic shock, and lymphoma metastasis:

1. Kavanaugh AF, davis LS, Nichols LA, Norris SH, Rothlein R, Scharschmidt LA, Lipsky PE. Treatment of refractory rheumatoid arthritis with a monoclonal antibody to intercellular adhesion molecule 1. Arthritis and Rheumatism. 37:992-9, 1994.

2. Rabb HA, Olivenstien R, Issenkutz TB, Renzi PM, Martin JG. The role of the leukocyte adhesion molecules VLA-4, LFA-1, and Mac-1 in allergic airway responses in the rat. Am J Respiratory and Critical Care Medicine 149:1186-91, 1994.

3. Winter S, Sweatman JJ, Hart A, Rhoades TH, **LARSON RS**. Role of LFA-1 mediated adhesion on survival of T-cell acute lymphoblastic lymphoma cells. Br J Hematol, 115:1-11,2001.

4. Bowes MP. Zivin JA. Rothlein R. Monoclonal antibody to the ICAM-1 adheison site reduces neurologic damage in rabiit cerebral embolism stroke model. Experimental Neurology 119:215-, 1993.

5. Aoudjit F, Patoworowski EF, Springer TA, St-Pierre Y. Protection from lymphoma Cell Metastasis in ICAM-1 mutant mice: A post homing event. J Immunol 161:2333-38, 1998.

6. Xu H, Gonzalo Y, St. Pierre Y, Williams IR, Kupper TS, Cotran RS, Springer TA, Gutierrez-Ramos, JC. Leukocytosis and resistance to septic shock in intercellular adhesion molecule-1 deficient mice. J Exp Med 180:95-101, 1994.

6. It is my opinion that, based on the attached exhibits, a person of skill in this field would reasonably expect the cyclic peptides to function as blockers of LFA-1/ICAM-1 function in any of a hematopoietic neoplastic disease, radiation injury, asthma, rheumatoid arthritis, or lymphoma metastasis, and that this activity is a basis for a pharmaceutical preparation of the cyclic peptides to be used in the treatment of those diseases or conditions.

7. All statements made in this Declaration of my own knowledge are true and all statements made in this Declaration on information and belief are believed to be true, and these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both under 18 U.S.C. 1001 and may jeopardize the validity of this application or any patent issuing thereon.

3/10/03
Date

Dr. Richard S. Larson

This document was signed before me on this 10th day of March, 2003.

Mary C. Archuleta, Notary Public
My commission expires 4/12/06

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(Case No. 03-275-A)

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Richard S. Larson	)
	) **Examiner: M. Haddad**
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Filing Date: January 16, 2001	) **Group Art Unit: 1644**
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Serial No. 09/760,599	)
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For: Peptide Inhibitors LFA-1/CAM-1 Interaction	)

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

POWER OF ATTORNEY BY ASSIGNEE OF ENTIRE INTEREST
(REVOCATION OF PRIOR POWERS)

As assignee of record of the entire interest of the above identified

☒ application

☐ patent

REVOCATION OF PRIOR POWERS OF ATTORNEY

all powers of attorney previously given in this patent, and in all applications and patents assigned to the Science & Technology Corporation @ UNM, are hereby revoked and

NEW POWER OF ATTORNEY

The undersigned hereby appoints all of the practitioners associated with the Customer Number provided below to prosecute this application, and all applications and patents assigned to, Science & Technology Corporation @ UNM, and to transact all business in the Patent and Trademark Office connected therewith and directs that all correspondence be addressed to that Customer Number:

Customer Number: **020306**
Principal attorney or agent: John J. McDonnell
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EVIDENCE AND CERTIFICATION OF CHAIN OF TITLE

☒ Recorded in PTO on April 6, 2001

Reel 011708
Frame 0381

☐ Recorded herewith.

ASSIGNEE CERTIFICATION

In accordance with 37 C.F.R. § 3.73 the assignee hereby certifies that the evidentiary documents with respect to its ownership have been reviewed and that, to the best of assignee's knowledge and belief, title is in the assignee seeking to take this action.

Date: 4-2-03

Signature

Name: Peter Perna
Title: President and Chief Executive Office of
Science & Technology Corporation @ UNM

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